

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method of detecting and localizing malignant tumours and or their metastases in tissues, which in healthy condition do not contain disturbing substantial quantities of CCK-receptors, in the body of a human being, which comprises (i) administering to said human being a composition comprising, in a quantity sufficient for external imaging, a peptide of the general formula

H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp - Phe - R₂(I) [[5]] (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH, wherein

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group;
or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety;
or a conjugate thereof with avidin or biotin;
wherein:

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n = 0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration
and wherein said peptide may comprise pseudo peptide bonds;

said peptide being labelled with (a) a radioactive metal isotope selected from the group consisting of ^{99m}Tc, ²⁰³Pb, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ⁹⁷Ru, ⁶²Cu, ⁶⁴Cu, ⁵²Fe, ^{52m}Mn and ⁵¹Cr, or (b) with a paramagnetic metal atom selected from the group consisting of Cr, Mn, Fe, Co, Ni, Cu, Pr, Nd, Sm, Yb, Gd, Tb, Dy, Ho and Er, or (c) with a radioactive halogen isotope, selected from ¹²³I, ¹²⁴I, ¹²⁵I, ¹³¹I, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br and ⁸²Br, and thereupon (ii) subjecting said human being to external imaging, by radioactive scanning or by magnetic resonance imaging, to determine the

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targeted sites in the body of said human being in relation to the background activity, in order to allow detection and localization of said tumours in the body.

2. (Currently Amended) A method of intraoperatively detecting and localizing malignant tumours or their metastases in tissues, which in healthy condition do not contain disturbing substantial quantities of CCK-receptors, in the body of a human being, which comprises (i) administering to said human being a composition comprising, in a quantity sufficient for detection by a gamma detecting probe, a peptide of the general formula I as defined in claim 1
H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp - Phe - R₂(I) (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety;
or a conjugate thereof with avidin or biotin; wherein (Xaa)_n, Xbb, Xcc, Xdd, m, R₁, and R₂ have the same meanings as in claim 1,

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group;
(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m=0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n =0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and wherein said peptide may comprise pseudo peptide bonds;

said peptide being labelled with ¹⁶¹Tb, ¹²³I, or ¹²⁵I, ^{99m}Tc, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ⁶²Cu, ⁶⁴Cu, ^{52m}Fe, ⁵¹Cr and thereupon (ii), after allowing the active substance to be bound and taken up in said tumours and after blood clearance of radioactivity, subjecting said human being to a radioimmunodetection technique in the relevant area of the body of said human being, by using a gamma detecting probe.

3. (Currently Amended) A method for the therapeutic treatment of malignant tumours that express CCK-receptor or their metastases in tissues, which in healthy condition do not contain substantial quantities of CCK-receptors, in the body of a human being, which comprises administering to said human being a composition comprising, in a quantity effective for combating or controlling tumours, a peptide of the general formula I as defined in claim 1 H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp - Phe - R₂ (I) (SEQ ID NO:27) or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety; or a conjugate thereof with avidin or biotin; wherein (Xaa)_n, Xbb, Xcc, Xdd, m, R₁, and R₂ have the same meanings as in claim 1,

R₁ is a C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group;
(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n = 0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

said peptide being labelled with an isotope selected from the group consisting of ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu, ¹⁰⁵Rh, ¹¹¹Ag, ⁺²⁴I, ¹²⁵I, and ¹³¹I and ⁸²Br.

4. (Currently Amended) [[A]] The method as claimed in claims of claim 1, 2, or 3, characterized in that the wherein said tumours and the metastases thereof to be detected, localized or therapeutically treated their metastases are selected from the group consisting of Small Cell Lung Carcinoma, Medullary Thyroid Carcinoma, Breast Carcinoma, Stromal Ovarian Carcinoma and Muscle Sarcoma.

5. (Currently Amended) [[A]] ~~The method as claimed in of claim 1, 2, or 3 characterized in that the wherein said tumours and the metastasis thereof to be detected, localized or therapeutically treated their metastases~~ are selected from the group consisting of Small Cell Lung Carcinoma and Medullaiy Thyroid Carcinoma.

6. (Currently Amended) [[A]] ~~The method as claimed in claims of claim 1, 2, or 3, characterized in that wherein said peptide is selected from the group consisting of H-DTyr-Gly--Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:11), H-Asp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:2), H-Asp-Tyr-Nle-Gly-Trp-Nle-Asp--Phe-NH₂ (SEQ ID NO:3), H-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO :4), H-DAsp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:5) and H-Dpr-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:6) , and preferably is H Asp Tyr Nle Gly Trp Nle Asp Phe NH₂ or H DAsp Tyr Nle Gly Trp Nle Asp Phe NH₂ .~~

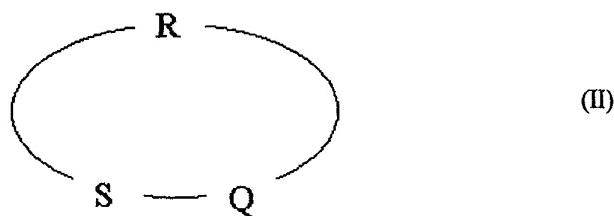
7. (Currently Amended) [[A]] ~~The method as claimed in claims of claim 1, 2, or 3 which comprises administering to said living being a composition comprising a labelled peptide as defined in said preceding claims, wherein said peptide is labelled with a radioactive halogen isotope selected from the group consisting of ¹²³I, ¹²⁴I, ¹²⁵I, ¹³¹I, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br and ⁸²Br, said radioactive halogen isotope being attached to a Tyr or Trp moiety of the peptide, or to the aryl group of substituent R₁.~~

8. (Currently Amended) [[A]] ~~The method as claimed in any of the preceding claims 1-3 of claim 1 which comprises administering to said living being a composition comprising a labelled peptide as defined in said preceding claims, wherein said peptide is labelled with a metal atom selected from (a) the group consisting of the radioactive isotopes ^{99m}Tc, ²⁰³Pb, ⁶⁶Ga, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ^{114m}In, ⁹⁷Ru, ⁶²Cu, ⁶⁴Cu, ⁵²Fe, ^{52m}Mn, ⁵⁴Cr, ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ^{117m}Sn, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁴⁹Tb, ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu, ¹⁰⁵Rh and ¹¹¹Ag, or (b) the group consisting of the paramagnetic metal atoms Cr, Mn, Fe, Co, Ni, Cu, Pr, Nd, Sm, Yb, Gd, Tb, Dy, Ho and Er;~~

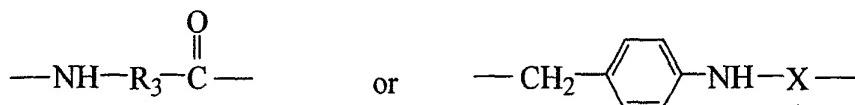
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said metal atom being radioactive metal isotope or said paramagnetic metal atom is attached to the peptide by means of a chelating group chelating said isotope or atom, which chelating group is bound by an amide bond or through a spacing group to the peptide molecule.

9. (Currently Amended) [[A]] The method as claimed in of claim 8, wherein said composition comprises a peptide labelled with a metal atom, chelated by an $N_tS_{(4-t)}$ tetradeятate chelating agent, wherein $t=2-4$, or by a chelating group derived from comprising ethylene diamine tetra-acetic acid (EDTA), diethylene triamine penta-acetic acid (DTPA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O' -bis(2-aminoethyl)-N,N,N',N' -tetraacetic acid (EGTA), N,N-bis(hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N''' -tetra-acetic acid (DOTA), hydroxyethylidiamine triacetic acid (HEDTA), 1,4,8,11 -tetra-azacyclo-tetradecane-N,N',N'',N''' -tetra-acetic acid (TETA), substituted DTPA, substituted EDTA, or from a compound of the general formula



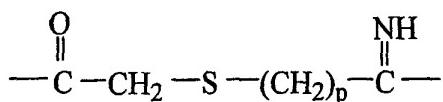
wherein S is sulfur, R is a branched or non-branched, optionally substituted hydrocarbyl radical, which may be interrupted by one or more hetero-atoms selected from N, O and S and/or by one or more NH groups, and Q is a group which is capable of reacting with an amino group of the peptide and which is preferably selected from the group consisting of carbonyl, carbimidoyl, N-(C₁-C₆)alkylcarbimidoyl, N-hydroxycarbimidoyl and N-(C₁-C₆)alkoxycarbimidoyl; and wherein said optionally present spacing group is a biotinyl moiety or has the general formula



(III)

(IV)

wherein R₃ is a C₁-C₁₀ alkylene group, a C₁-C₁₀ alkylidene group or a C₂-C₁₀ alkenylene group, and X is a thiocarbonyl group or a group of the general formula



(V)

wherein p is 1-5.

10. (Cancelled)

11. (Cancelled)

12. (Currently Amended) A pharmaceutical composition ~~to be used for the method as claimed in claim 1, 2 or 3,~~ comprising, in addition to a pharmaceutically acceptable carrier material and, if desired, at least one pharmaceutically acceptable adjuvant, as the active substance, in a quantity sufficient for external imaging, ~~respectively or~~ detection by a gamma detecting probe or for combating or controlling tumours, a peptide of the general formula I as defined in claim 1

H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp - Phe - R₂ (I) (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety;

or a conjugate thereof with avidin or biotin; wherein (Xaa)_n, Xbb, Xcc, Xdd, m, R₁, and R₂ have the same meanings as in claim 1,

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group;

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg,

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Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n = 0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and wherein said peptide may comprise pseudo peptide bonds;

said peptide being labelled with (a) a radioactive metal isotope selected from the group consisting of ^{99m}Tc, ²⁰³Pb, ⁶⁶Ga, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ^{114m}In, ⁹⁷Ru, ⁶²Cu, ⁶⁴Cu, ⁵²Fe, ^{52m}Mn, ⁵¹Cr, ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ^{117m}Sn, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁴⁹Tb, ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu, ¹⁰⁵Rh and ¹¹¹Ag, or (b) with a paramagnetic metal atom selected from the group consisting of Cr, Mn, Fe, Co, Ni, Cu, Pr, Nd, Sm, Yb, Gd, Tb, Dy, Ho and Er, or (c) with a radioactive halogen isotope, selected from ¹²³I, ¹²⁴I, ¹²⁵I, ¹³¹I, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br and ⁸²Br.

13. (Currently Amended) [[A]] The composition as claimed in of claim 12, characterized in that the wherein said active substance is a derivatized peptide selected from the group consisting of DTPA-Asp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:19), DTPA-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:20), DTPA-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:21), DTPA-DAsp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:22) and Dpr(β-DTPA)-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:23), wherein said derivatized peptide being is labelled with a metal isotope or atom as defined in claim 8 attached to the peptide by means of a chelating group chelating said isotope or atom, which chelating group is bound by an amide bond or through a spacing group to the peptide molecule.

14 (Currently Amended). [A] The composition as claimed in of claim 13, characterized in that wherein said derivatized peptide is DTPA-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:20) or DTPA-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₇ (SEQ ID NO:21)

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15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (Cancelled)

22. (Cancelled)

23. (New) The method of claim 2 wherein said ^{161}Tb , $^{99\text{m}}\text{Tc}$, ^{67}Ga , ^{68}Ga , ^{72}As , ^{111}In , $^{113\text{m}}\text{In}$, ^{62}Cu , ^{64}Cu , ^{52}Fe , $^{52\text{m}}\text{Mn}$ or ^{51}Cr is attached to the peptide by means of a chelating group chelating said ^{161}Tb , $^{99\text{m}}\text{Tc}$, ^{67}Ga , ^{68}Ga , ^{72}As , ^{111}In , $^{113\text{m}}\text{In}$, ^{62}Cu , ^{64}Cu , ^{52}Fe , $^{52\text{m}}\text{Mn}$ or ^{51}Cr which chelating group is bound by an amide bond or through a spacing group to the peptide molecule.

24.(New) The method of claim 3 wherein said isotope is attached to the peptide by means of a chelating group chelating said isotope, which chelating group is bound by an amide bond or through a spacing group to the peptide molecule.

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25. (New). A pharmaceutical composition comprising, in addition to a pharmaceutically acceptable carrier material and, optionally, at least one pharmaceutically acceptable adjuvant, as the active substance, in a quantity sufficient for detecting and localizing malignant tumours, a peptide selected from the group consisting of [¹²⁵I-D-Tyr]-Gly-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO: 13) and D-Tyr-Gly-Asp-[¹²⁵I-Tyr]-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ IDNO:14).

26. (New) A labelled peptide of the general formula

H-(Xaa)_n- (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp - Phe - R₂(I) (SEQ ID NO:27) or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH, wherein

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety; or a conjugate thereof with avidin or biotin; wherein:

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n =0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and wherein said peptide may comprise pseudo peptide bonds;

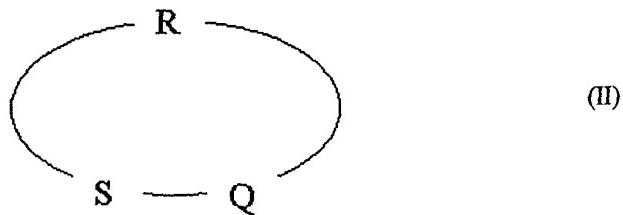
said peptide being labelled with (a) a radioactive metal isotope selected from the group consisting of ^{99m}Tc, ²⁰³Pb, ⁶⁶Ga, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ^{114m}In, ⁹⁷Ru, ⁶²Cu, ⁶⁴Cu, ⁵²Fe, ^{52m}Mn, ⁵¹Cr, ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ^{117m}Sn, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁴⁹Tb, ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu,

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^{105}Rh and ^{111}Ag , or (b) with a paramagnetic metal atom selected from the group consisting of Cr, Mn, Fe, Co, Ni, Cu, Pr, Nd, Sm, Yb, Gd, Tb, Dy, Ho and Er, or (c) with a radioactive halogen isotope, selected from ^{123}I , ^{124}I , ^{125}I , ^{131}I , ^{75}Br , ^{76}Br , ^{77}Br and ^{82}Br .

27. (New) The labelled peptide of claim 26 wherein said metal isotope or said metal atom is attached to the peptide by means of a chelating group chelating said metal isotope or said metal atom, which chelating group is bound by an amide bond or through a spacing group to the peptide molecule.

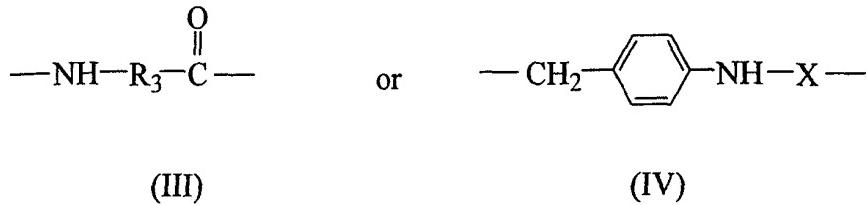
28. (New) The labelled peptide of claim 26 wherein said metal isotope or said metal atom is attached to the peptide by means of a chelating group chelating said metal isotope or said metal atom, wherein said chelating group is a tetradeinate chelating agent or comprises ethylene diamine tetra-acetic acid (EDTA), diethylene triamine penta-acetic acid (DTPA), cyclohexyl 1,2-diamine tetra-acetic acid (CDTA), ethyleneglycol-O,O'-bis(2-aminoethyl)-N,N,N',N'-tetraacetic acid (EGTA), N,N-bis(hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetra-acetic acid (DOTA), hydroxyethyldiamine triacetic acid (HEDTA), 1,4,8,11-tetra-azacyclo-tetradecane-N,N',N'',N'''-tetra-acetic acid (TETA), substituted EDTA, or from a compound of the general formula



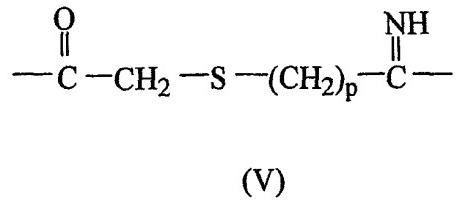
wherein S is sulfur, R is a branched or non-branched, optionally substituted hydrocarbyl radical, which may be interrupted by one or more hetero-atoms selected from N, O and S and/or by one or more NH groups, and Q is a peptide and which is selected from the group consisting of carbonyl, carbimidoyl, -(C₁-C₆)alkylcarbimidoyl, N-hydroxycarbimidoyl and N-(C-

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C₆)alkoxycarbimidoyl; and wherein said optionally present spacing group is a biotinyl moiety or has the general formula



wherein R₃ is a C₁-C₁₀ alkylene group, a C₁-C₁₀ alkylidene group or a C₂-C₁₀ alkenylene group, and X is a thiocarbonyl group or a group of the general formula



wherein p is 1-5.

29. (New) The labelled peptide of claim 26 wherein said peptide comprises DTPA and is selected from the group consisting of DTPA-Asp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:19), DTPA-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:20), DTPA-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID N0:21), DTPA-DAsp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH₂ (SEQ ID NO:22) and Dpr(β-DTPA)-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID N0:23).

30. (New) The labelled peptide of claim 26 wherein said peptide comprises DTPA and is selected from the group consisting of DTPA-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:20) and DTPA-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:21).

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31. (new) A method for preparing a labelled peptide of general formula

H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp- Phe - R₂ (I) (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and
R₁COOH, wherein

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group;
or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H
group of another amino acid moiety;
or a conjugate thereof with avidin or biotin; wherein:

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are
selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg,
Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n =0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and
wherein said peptide may comprise pseudo peptide bonds;

said peptide being labelled with (a) a radioactive metal isotope selected from the group
consisting of ^{99m}Tc, ²⁰³Pb, ⁶⁶Ga, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ^{114m}In, ⁹⁷Ru, ⁶²Cu ⁶⁴Cu, ⁵²Fe,
^{52m}Mn, ⁵¹Cr, ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ^{117m}Sn, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au,
¹⁴⁹Tb ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu,
¹⁰⁵Rh and ¹¹¹Ag, or (b) with a paramagnetic metal atom selected from the group consisting of Cr,
Mn, Fe, Co, Ni, Cu, Pr, Nd, Sm, Yb, Gd, Tb, Dy, Ho and Er, or (c) with a radioactive halogen
isotope, selected from ¹²³I, ¹²⁴I, ¹²⁵I, ¹³¹I, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br and ⁸²Br;

wherein said peptide comprises a chelating group bound by an amide bond or through a spacing
group to said peptide;

said method comprising reacting said peptide with said metal isotope or said metal atom in the
form of a salt or of a chelate, bound to a comparatively weak chelator, to form a complex.--

Preliminary Amendment
Inventors: Jean-Claude Reubi
S.N.: 10/626,229

32. (New) A kit for preparing a radiopharmaceutical composition, comprising (i) a derivatized peptide of general formula

H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp- Phe - R₂ (I) (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH, wherein

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety;
or a conjugate thereof with avidin or biotin;
wherein:

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n =0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and wherein said peptide may comprise pseudo peptide bonds;

to which derivatized peptide, if desired, an inert pharmaceutically acceptable carrier and/or formulating agents and/or adjuvants is/are added, (ii) a solution of a salt or chelate of a metal selected from the group consisting of the radioactive isotopes ^{99m}Tc, ²⁰³Pb, ⁶⁶Ga, ⁶⁷Ga, ⁶⁸Ga, ⁷²As, ¹¹¹In, ^{113m}In, ^{114m}In, ⁹⁷Ru, ⁶²Cu ⁶⁴Cu, ⁵²Fe, ^{52m}Mn, ⁵¹Cr, ¹⁸⁶Re, ¹⁸⁸Re, ⁷⁷As, ⁹⁰Y, ⁶⁷Cu, ¹⁶⁹Er, ^{117m}Sn, ¹²¹Sn, ¹²⁷Te, ¹⁴²Pr, ¹⁴³Pr, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁴⁹Tb ¹⁶¹Tb, ¹⁰⁹Pd, ¹⁶⁵Dy, ¹⁴⁹Pm, ¹⁵¹Pm, ¹⁵³Sm, ¹⁵⁷Gd, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁷²Tm, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁷⁷Lu, ¹⁰⁵Rh and ¹¹¹Ag, and (iii) instructions for use with a prescription for reacting the ingredients present in the kit.

Preliminary Amendment
Inventors: Jean-Claude Reubi
S.N.: 10/626,229

33. (New) A kit for preparing a radiopharmaceutical composition, comprising (i) a derivatized peptide of general formula:

H - (Xaa)_n - (Xbb)_m - Tyr - Xcc - Gly - Trp - Xdd - Asp- Phe - R₂ (I) (SEQ ID NO:27)
or an acid amide thereof, formed between a free NH₂-group of an amino acid moiety and R₁COOH, wherein

R₁ is a (C₁-C₃)alkanoyl group, an arylcarbonyl group, or an aryl-(C₁-C₃)alkanoyl group; or a lactam thereof, formed between a free NH₂ group of an amino acid moiety and a free CO₂H group of another amino acid moiety;
or a conjugate thereof with avidin or biotin; wherein:

(Xaa)_n stands for 0 to 25 amino acid moieties which are equal or different and are selected from Ala, Leu, Asn, Dpr, Gln, Glu, Ser, Ile, Met, His, Asp, Lys, Gly, Thr, Pro, Pyr, Arg, Tyr, Trp, Val and Phe;

m = 0 or 1;

Xbb is Asp, Dpr, Glu or Pyr; with the proviso that Xbb can only be Pyr when n =0;

Xcc is Met, Leu or Nle;

Xdd is Met, Leu or Nle; and

R₂ is a hydroxy group, an acetoxy group or an amino group;

wherein one or more of the amino acids of said peptide can be in the D-configuration and wherein said peptide may comprise pseudo peptide bonds;

to which derivatized peptide, if desired, an inert pharmaceutically acceptable carrier and/or formulating agents and/or adjuvants is/are added, (ii) a reducing agent, and, if desired, a chelator, said ingredients (i) and (ii) optionally being combined, and (iii) instructions for use with a prescription for reacting the ingredients of the kit with ^{99m}Tc in the form of a pertechnetate solution or with ¹⁸⁶Re or ¹⁸⁸Re in the form of a perrhenate solution.

34. (New) The method of claim 1, 2, or 3, wherein said peptide is selected from the group consisting of H-Asp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:3) and H-DAsp-Tyr-Nle-Gly-Trp-Nle-Asp-Phe-NH₂ (SEQ ID NO:4).

Preliminary Amendment
Inventors: Jean-Claude Reubi
S.N.: 10/626,229

35. (New) The method of claim 2 wherein said peptide is labelled with a radioactive halogen isotope selected from the group consisting of ^{123}I and ^{125}I , said radioactive halogen isotope being attached to a Tyr or Trp moiety of the peptide, or to the aryl group of substituent R₁.

36. (New) The method of claim 3 wherein said peptide is labelled with a radioactive halogen isotope selected from the group consisting of ^{125}I , ^{131}I and ^{82}Br , said radioactive halogen isotope being attached to a Tyr or Trp moiety of the peptide, or to the aryl group of substituent R₁.